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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,279	KLOCK ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/20/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/20/2008 has been entered.

Claim Status

Claims 1 and 8-20 are pending. Claims 2-7 are cancelled. Claim 1 is amended. Claims 17-20 are newly added. Claims 1 and 8-20 are under current examination.

Priority

This application claims benefit from as a 371 of PCT/EP04/14097 (filed 12/10/2004). In addition, the application claims benefit from foreign application GERMANY DE 103 58 407.2 (filed 12/11/2003). The instant application has been granted the benefit date, 10 December 2004, from the application PCT/EP04/14097.

RESPONSE TO ARGUMENTS

Written Description (35 USC 112, first paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-12, and 14-16 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Furthermore, the pending rejection is extended to reject claim 17. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments (Remarks, page 4-7) and claim amendments, filed 20 November 2008, with respect to claims 1, 8-12 and 14-16 rejected under 35 USC 112, 1st paragraph (written description) have been fully considered but they are unpersuasive. The examiner has also applied the written description analysis of previously rejected 1, 8-12 and 14-16 to newly added claim 17.

The applicant has amended the instant claims. Newly amended claim 1 is directed to an isolated nucleic acid having a nucleic acid sequence of at least 80% sequence identity to SEQ ID NO:1 or SEQ ID NO:2 which is anti-apoptotically active.

In the previous rejection, the examiner had argued that there is inadequate description of the structure-function relationship, particularly which domains of the

claimed sequences must be conserved or conservatively mutated to maintain the anti-apoptotic activity. The applicant traverses this view and offers remarks in support of his position that there is sufficient written description for the instant claims. In particular, the applicant argues, that SEQ ID NOs: 2 and 4 were tested for anti-apoptotic activity. SEQ ID NO:2 (66 nucleotides) and SEQ ID NO:4 (58 nucleotides) share a core structure which is 100% identical for 53 nucleotides. The difference between SEQ ID NO:2 and SEQ ID NO:4 occurs in the 13 bases at the 3' end of the molecules. Therefore, the entire analysis of which portions of SEQ ID NO:2 which can be varied and maintain anti-apoptotic activity was performed on the 20% of SEQ ID NO:2 which is located in the 3' end. The breadth of the claims encompasses alterations throughout the molecule. In addition, the applicant indicates "applicants have provided a postulated secondary structure of SEQ ID NO:2, and have identified that structure H1 may be important but that helix F may not. The experiments comparing the apoptotic activity of SEQ IDNO:2 and SEQ ID NO:4 address the importance of helix F, indicating that helix F does not need to be present" (Remarks, page 7, lines 5-7). These comments leave open to speculation as to what features are important for the anti-apoptotic activity. It seems the applicant has not adequately described which portion of SEQ ID NO:2 is required for anti-apoptotic activity, but has determined that helix F may not be important for anti-apoptotic activity. Because of the limited description of which portions of SEQ ID NO:2 are required for anti-apoptotic activity and the importance of this functional language to the claimed genus, the examiner finds the applicant's argument unpersuasive. The

examiner concludes there is insufficient written description of the claimed genus of nucleic acids.

The examiner reiterates the pending rejection, with some modifications:

Claims 1, 8-12, and 14-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The instant claims encompass a genus of nucleic acids having at least 80% to identity to SEQ ID NO:1-2 and having anti-apoptotic activity of at least 70%, 80%, 90% and 95% inhibition. Under the new Written Description Guidelines (March 25, 2008, Revision 1) the examiner is directed to determine whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing. The following considerations are critical to this determination:

a. Actual Reduction to Practice. In the instant case, the specification shows two embodiments, SEQ ID NO:2 (aptamer 89) and SEQ ID NO:4 (aptamer 89-2) which are reduced to practice. Both of these sequences showed anti-apoptotic activity in assays provided in the specification (Examples 6-7, Table 2).

b. Disclosure of structure. The applicant has provided sequence listings of SEQ ID NO:1 (DNA), SEQ ID NO:2 (RNA) and SEQ ID NO:4 (RNA). SEQ ID NO:2 (66 nucleotides) and SEQ ID NO:4 (58 nucleotides) share a core structure which is 100% identical for 53 contiguous nucleotides. Additionally, with the help of a computer, a skilled artisan could identify all nucleic acids which are at least 80% identical to the full length sequence of SEQ ID NO:1 or 2. However, neither the specification nor the art indicate a relationship between the structure of the claimed genus of nucleic acids and

the recited anti-apoptotic activity. In particular, there is no indication in the art or specification as to the effect of varying up to 20% of the nucleic acids of the claimed genus of isolated on the anti-apoptotic function of the nucleic acids that are not 100% identical to SEQ ID NO:1, 2, or 4.

c. Sufficient relevant identifying characteristics. As mentioned in "b" above, the complete sequence of SEQ ID NO:1, 2, and 4 are provided. Furthermore, the functional characteristics of these sequences have been demonstrated in Examples 6-7 (Spec., pages 17-18). These sequences demonstrate anti-apoptotic activity. The specification indicates, "Anti-apoptotically active, in the sense of the present invention, means that the corresponding substance in the inhibition test according to Example 6, causes an inhibition index of at least 50%, preferably at least 60%, especially preferably at least 70%, even more preferably at least 80%, even more preferably still at least 90% and most preferably of all at least 95 % in relation to the control with TSP-l-induced apoptosis." (page 6, line 28 to page 7, line 2). Because of the specification's description of assays for testing anti-apoptotic activity and the specification's narrow definition of the activity being measured in Examples 6-7, it seems that a skilled artisan would be clearly able to test a genus of polynucleotides having at least 80% identity to SEQ ID NO:1-2.

However, the new written description guidelines indicate in Examples 10 and 11A that without disclosure about which nucleotides can vary from SEQ ID NO:1 or 2 and still retain the claimed activity, the examiner should conclude that the applicant was not in possession of the claimed genus of isolated nucleic acids based on disclosure of the

limited species of SEQ ID NO:1, 2 or 4. SEQ ID NOs: 2 and 4 were found to have anti-apoptotic activity. SEQ ID NO:2 (66 nucleotides) and SEQ ID NO:4 (58 nucleotides) share a core structure which is 100% identical for 53 nucleotides. The difference between SEQ ID NO:2 and SEQ ID NO:4 occurs in the 13 bases at the 3' end of the molecules. Therefore, the entire analysis of which portions of SEQ ID NO:2 which can be varied and maintain anti-apoptotic activity was performed on the 20% of SEQ ID NO:2 which is located in the 3' end. The breadth of the claims encompasses alterations throughout the molecule. Therefore, the examiner concludes there is limited description of the structure-function relationship between nucleic acid molecule having at least 80% identity to SEQ ID NO:2 and their anti-apoptotic activity and the examiner further concludes a skilled artisan would find the specification inadequately describes the nucleic acids encompassed by the claimed genus.

d. The method of making the claimed invention is well established.

e-f. The level of skill in the art, and the predictability in the art are all well established and/or very predictable to a skilled artisan, with regard to generating the genus of polynucleotides having at least 80% to SEQ ID NO:1 or 2. Likewise, screening such a genus would be easy for a skilled artisan. However, predicting which nucleotides can be varied from SEQ ID NO:1 or 2 and still retain anti-apoptotic activity would be unpredictable, based on the state of the art and the instant application.

Therefore, the examiner concludes that there is insufficient written description of the instantly claimed genus.

SEQ ID NO:1, 2 and 4 are free of the art. Additionally, no prior art was found that discloses a sequence having 80% identity to the full length sequence of SEQ ID NO:1 or SEQ ID NO:2.

Therefore, the rejection of claims 1, 8-12, and 14-17 under 35 USC 112, 1st paragraph (written description) is maintained for the reasons of record and the comments above.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some 'experimentation.'" Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention.

"Whether undue experimentation is needed is not a single simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

SCOPE OF THE INVENTION

The breadth of the claims encompasses a genus of nucleic acids having at least 80% to identity to SEQ ID NO:1 or 2 and having anti-apoptotic activity of at least 90% (claim 11) and 95% inhibition (claim 12).

GUIDANCE & WORKING EXAMPLES

The specification teaches SEQ ID NO: 2 was found to have anti-apoptotic activity of 91% inhibition (Table 2). The specification teaches SEQ ID NO: 4 was found to have anti-apoptotic activity of 83% inhibition (Table 2). SEQ ID NO:2 (66 nucleotides) and SEQ ID NO:4 (58 nucleotides) share a core structure which is 100% identical for 53 nucleotides. Therefore, SEQ ID NO:4 is at least 80% identical to SEQ ID NO:2. Accordingly, SEQ ID NO:4 is at least 80% identical to SEQ ID NO:2, but has

anti-apoptotic activity of only 83% inhibition. While SEQ ID NO:4 meets the structural limitations of claims 11-12, it does not meet the functional limitations. Therefore, the specification does not provide sufficient guidance on how to make the nucleic acids of claims 11-12.

QUANTITY OF EXPERIMENTATION

The guidance of the specification contradicts the claim limitations of claims 11-12 for at least one embodiment, SEQ ID NO: 4. Consequently, there is ample reason to conclude that there would be a high degree of unpredictability in making the genus of nucleic acids encompassed by claims 11-12.

CONCLUSION

In conclusion, given the breadth of the claims and because the guidance of the specification contradicts the claim limitations of claims 11-12, an undue quantity of experimentation is require to make and/or use the invention of claims 11-12.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Morris (WO2003/039484, published 15 May 2003). Morris teaches SEQ ID NO:16, an isolated nucleic acid comprising a portion of instant SEQ ID NO:1 encompassing the dinucleotide "CC."

The instant claims recite "***an*** isolated nucleic acid having ***a*** sequence of SEQ ID NO:1." According to Technology Center 1600 procedure the examiner is instructed to interpret this type of claim language broadly: Claim language such as claims 13 and 18 encompasses nucleic acids that comprise the full-length sequence of SEQ ID NO: 1 or any portion of SEQ ID NO: 1. This claim is anticipated by any nucleic acid comprising any dinucleotide or larger oligonucleotide which is a portion of SEQ ID NO:1.

If the claim 13 were amended to recite "An isolated nucleic acid having **a *the*** nucleic sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:2," the examiner would interpret the claims to encompass only nucleic acids that comprise the full length of SEQ ID NO: 1 (or SEQ ID NO:2), with or without additional nucleotides at either or both ends. Such language would not be anticipated by the cited prior art.

If the claim 18 were amended to recite "An isolated nucleic acid ~~having a~~ ***wherein the*** nucleic sequence ~~of~~ ***is*** at least 90% ~~sequence identity~~ ***identical*** to SEQ ID NO:1 or SEQ ID NO:2," the examiner would interpret the claims to encompass only nucleic acids that comprise 90% identity to the full length of SEQ ID NO: 1 (or SEQ ID NO:2), with or without additional nucleotides at either or both ends. Such language would not be anticipated by the cited prior art. It is also suggested that claim 19 be amended in a similar way.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-12 recite the limitation "an" in the first word of the instant claims. There is insufficient antecedent basis for this limitation in the claim. Appropriate correction is requested.

Conclusion

Claims 1 and 8-20 are rejected.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633